REMARKS/ARGUMENTS

Claims 1-13, 16, 17, 21-23, 30, 31, 34 and 36 were pending before this communication. Claims 1-12 are directed to non-elected inventions, and have been canceled in the present amendment. Additionally, claims 17 and 31 have been canceled without prejudice for prosecution in a continuing application and without acquiescence to any rejection of record.

Claims 16 and 23 have been amended to define Applicants' invention with greater particularity. These amendments are identical to those previously presented with the response filed April 6, 2004. These amendments add no new matter as they are fully supported by the specification and original claims. Applicants reserve the right to pursue non-elected subject matter in a continuing application without prejudice.

Telephonic Interview of May 4, 2004

Applicants thank Examiner Kam for the courtesy of a telephonic interview with the undersigned and Andrew Cubitt of X-Ceptor Therapeutics, Inc., the assignee of record in the instant application. The Advisory Action mailed April 20, 2004 was discussed during the interview. Applicants indicated their confusion as to the denial of entry of amendments to the claims, where the cancellation of non-elected subject matter reduced issues, including an objection of record as discussed below. Examiner Kam indicated that she would reconsider the entry of the amendments to the claims.

Applicants also clarified the situation with respect to the pending claims and the rejection of record under 35 U.S.C. § 112, first paragraph. In particular, Applicants pointed out that the invention was directed to the use of LXR agonists based on their ability to affect glucose metabolism. This is in contrast to much of the Examiner's stated positions to date, which focused on the use of LXR agonists in relation to lipid metabolism. Additionally, Applicants pointed out that the Examiner's emphasis on an alleged lack of "structure/function" relationship was misplaced because LXR agonists of various structures are known and it is the functionality of being an LXR agonist, rather than any particular compound structure, which is the basis for

the claimed invention's ability to affect glucose metabolism. Further discussion of Applicants' position are provided below.

Objections to Claims

Claims 16 and 23 have been objected to because the claim allegedly refers to non-elected additional active agents. Applicants respectfully traverse the objection, but have amended the claims in order to reduce issues and to expedite the allowance of the present application. Applicants accordingly request withdrawal of the objection. Applicants reserve the right to pursue non-elected subject matter in a continuing application without prejudice.

Issues under 35 U.S.C. §112 First Paragraph

Claims 13, 16, 17, 21-23, 30, 31, 34 and 36 have been rejected under 35 U.S.C. §112, first paragraph as allegedly not enabled such that a skilled artisan could make and/or use the invention commensurate in scope with the claims. The Examiner alleges (see page 4 of the Office Action) that while the specification is enabling for a method of treating diabetes type II comprising administering a specific LXR agonist, (compound 1), the specification does not reasonably provide enablement for a method for treating, or reducing the risk of developing or recurrence of diabetes, with the disclosed compound, or treating type II diabetes wherein the structure of the LXR agonist is not defined.

Additionally, the Advisory Action asserts that the dosages necessary to use LXR agonists of structures other than the compound used in the Example section of the instant application; and that the claims encompass the use of unspecified LXR agonists.

Applicants respectfully traverse the rejection on the grounds that the currently pending claims are fully enabled by the present specification and the knowledge of the skilled practitioner. Accordingly, no *prima facie* case of non-enablement is present.

As an initial matter, Applicants point out that claims 17 and 31 are no longer pending because the remaining claims are better tailored to currently contemplated,

commercially relevant, embodiments of the invention. The cancellation of claims 17 and 31 is thus not in acquiescence to the instant rejection.

Additionally, and as noted above, the instant invention is based on the discovery of the effect of LXR agonists on glucose metabolism. Thus, Applicants respectfully submit that the Examiner's reliance on information regarding LXR agonist activity in relation to lipid metabolism is misplaced. The fact that LXR agonists have been defined or characterized in the past in relation to lipid metabolism does not negate or alter the discovery that the agonists may be effectively used to decrease hyperglycemia and insulin resistance as provided by the instant disclosure and application.

With respect to the possible concern and emphasis regarding the scope of the claims, Applicants point out that the fact that the claims encompass the use of "LXR agonists" without recitation of particular structures raises **no** issue of undue experimentation. As noted during the telephonic interview and in the response filed October 16, 2003 (mailed October 13, 2003), LXR agonists of various structures are known (see pages 9 and 10 of the response filed October 16, 2003). The allegation that enablement is limited to particular structures which function as LXR agonists is misplaced because the agonists are claimed, and act, by virtue of their ability to function as an LXR agonist. It is the use of this activity, rather than any particular structure, which is claimed as the invention. Since it is the activity that supports the use of the agonists in relation to glucose metabolism, it is entirely proper (and permitted[1]) to claim the agonists by function rather than structure. Moreover, and as the Examiner no doubt appreciates, enablement does not require the recitation of that which is known in the art, such as the identities and structures of compounds already known as LXR agonists.

Moreover, and to assist the Examiner in advancing the prosecution of the instant application, attached is a copy of Cao, *et al.* ("Antidiabetic action of a liver X receptor agonist mediated by inhibition of hepatic gluconeogenesis", J. Biol. Chem. 278(2):1131-1136, 2003). While this article was published after the filing date of the instant application, it may nevertheless be used to support Applicants' position that LXR agonists can be used to decrease

[1] See MPEP 2173.05(g) and the cases cited therein.

hyperglycemia, and thus treat diabetes and insulin resistance. The article provides a possible mechanism by which LXR agonists act.

Cao *et al.* describe the effects of T0901317, an LXR agonist with a structure wholly distinct from the compound described in the instant application. But both compounds reduce plasma glucose levels (see Figure 15 of the instant application and Cao *et al.*'s abstract and Figure 1a). Additionally, they demonstrate that their compound improves insulin sensitivity in insulin resistant rats (see abstract and Figure 1b). Figures 1a and 1b also show these effects to be dose dependent, while Figure 1c shows that treatment of normal mice resulted in no significant change in plasma glucose levels.

Cao *et al.* further state that their LXR agonist "exerts antidiabetic effects through suppression of the hepatic gluconeogenic process." (see pages 1134-1135, bridging paragraph). They further state that "LXR activation alters liver metabolism in a manner reminiscent of insulin" to decrease gluconeogenesis (see page 1136, left column, second paragraph). They summarize their findings by noting that use of LXR agonists can lead to "a significant reduction in hyperglycemia and an improvement in insulin sensitivity" (see page 1136, left column, third paragraph).

Based on the above, and as previously presented by Applicants, there is simply no objective reason to doubt the fact that LXR agonists may be used to treat diabetes by decreasing hyperglycemia and/or reducing insulin resistance. Accordingly, there is no objective reason to limit the claims to only treatment of type II diabetes with a single compound.

As for the reliance on an alleged need to define dosages for the use of additional LXR agonists, Applicants respectfully submit that no issue of undue experimentation is present. As noted during the telephonic interview, it is well settled that undue experimentation is not the absence of experimentation.[2] Undue experimentation is also not the possible need for experimentation to find a previously unknown answer. On the other hand, it is also well settled that routine and repetitive experimentation is not undue. Applied to the situation of additional LXR agonists, Applicants respectfully point out that no more than routine or repetitive

[2] *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

experimentation is needed to determine dosages for various agonists. This is supported by the dose dependent effects on plasma glucose levels shown by Cao *et al.* and as noted above. Additionally, Figure 15 of the instant application demonstrates how routine it is to determine effective dosages for reducing plasma glucose levels. A given LXR agonist at a give dosage can be administered and compared to a control to observe the effects on plasma glucose levels over time (see Figure 15). Applicants respectfully submit that a person skilled in the art can thus experiment with a variety of LXR agonists at a variety of dosages to identify suitable dosages without undue experimentation.

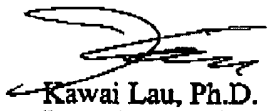
In light of the foregoing, Applicants strongly submit that no issue of undue experimentation, and thus lack of enablement, exists with respect to pending claims 13, 16, 21-23, 30, 34 and 36. Accordingly, this rejection should be withdrawn and the claims indicated as allowable.

CONCLUSION

Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is urged.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6151 .

Respectfully submitted,



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